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Dr. Bopanna KM
Associate Professor,
Department of Paediatrics,
Akash Institute of Medical
Sciences Devanahalli,
Bangalore, Karnataka, India

Corresponding Author:
Dr. Bopanna KM
Associate Professor,
Department of Paediatrics,
Akash Institute of Medical
Sciences Devanahalli,
Bangalore, Karnataka, India

Determination of cases of neutropenia in 104 children

Dr. Bopanna KM

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Abstract

Background: Neutropenia, usually defined as an absolute neutrophil count below $1.5 \times 10^9/L$, encompasses a wide range of diagnoses, from normal variants to life-threatening acquired and congenital disorders. The present study evaluated cases of neutropenia and fever in children.

Materials & Methods: 104 children confirmed case of fever and neutropenia of both genders Were studied.

Results: Age group 10-12 years had 14 boys and 8 girls, 12-14 years had 20 boys and 10 girls and 14-16 years had 30 boys and 12 girls. The main cause of neutropenia was bacterial in 54, viral in 20, fungal in 15, drugs in 10 and autoimmune in 5 cases. The difference was significant ($P < 0.05$). Out of 104 patients, 98 survived and 6 died. The difference was significant ($P < 0.05$).

Conclusion: Authors found that maximum cases were seen in boys and age group 14-16 years.

Keywords: children, fever, neutropenia

Introduction

Neutropenia, usually defined as an absolute neutrophil count (ANC) below $1.5 \times 10^9/L$ ($1500/mm^3$), encompasses a wide range of diagnoses, from normal variants to life-threatening acquired and congenital disorders^[1]. The functional consequences depend largely, but not exclusively, on the severity of neutropenia: ANC of $1.0-1.5 \times 10^9/L$ does not impair host defense, but may warrant investigation of the underlying cause; ANC of $0.5-1.0 \times 10^9/L$ may slightly increase the risk of infections, but only if other arms of the immune system are impaired; ANC of $0.2-0.5 \times 10^9/L$ is associated with an increased risk of infections in most patients. ANC of $0.2 \times 10^9/L$ or less (often referred to as "agranulocytosis") carries a risk of severe, life-threatening infections with susceptibility to opportunistic organisms^[2].

Despite a considerable reduction over the past decades in infection-related mortality in patients with cancers who present with fever and neutropenia (FN), infections remain a major cause of morbidity and mortality in this susceptible population. The strategy of using empiric antibiotics has greatly influenced the outcome of fever in a neutropenic host^[3].

It is important to note that blood neutrophil counts are not as stable as other blood cell counts or many other physiological measurements. Counts may vary considerably over short periods of time, associated with activity, exercise, eating or just the time of day. Counts vary even more with serious infections, inflammatory disorders, corticosteroid therapy or extreme anxiety^[4]. It is always important in the evaluation of blood neutrophil counts to consider the conditions when the blood sample was obtained and to have several measurements when defining the severity of acute or chronic neutropenia. Neutropenia can be described as transient (or "acute") or chronic (or "persistent"); extrinsic or intrinsic; by descriptive names (e.g., neonatal isoimmune neutropenia of infancy, cyclic neutropenia, severe congenital neutropenia) and as syndromes (e.g., Kostmann, Shwachman-Diamond, and Barth syndromes). The discovery of the diverse causes for the congenital neutropenias now permits genetic diagnosis in many cases^[5]. The present study evaluated cases of neutropenia and fever in children.

Materials & Methods

The present study comprised of 104 children confirmed case of fever and neutropenia of both genders. Fever was defined as a single oral temperature of $\geq 38.3^\circ C$ or an oral temperature of $\geq 38.0^\circ C$ that persists for over one hour. Neutropenia was defined as an ANC ≤ 500 cells/mm³. All were included in the study after obtaining their written consent.

Data such as name, age, gender etc. was recorded. A thorough clinical examination was performed. Duration of fever, days of hospitalization and mortality rate was recorded. Results of the study was compiled and entered in MS sheet for statistical analysis. Chi- square test and Mann Whitney U test was used for analysis. P value less than 0.05 was considered significant.

Results

Table 1: Distribution of patients

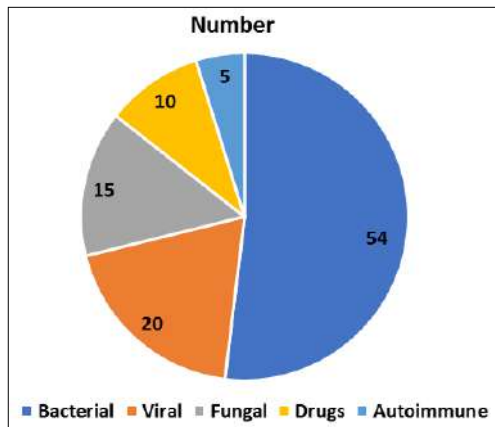
Age group (Years)	Boys	Girls
10-12	14	8
12-14	20	10
14-16	30	12

Table I shows that age group 10-12 years had 14 boys and 8 girls, 12-14 years had 20 boys and 10 girls and 14-16 years had 30 boys and 12 girls.

Table 2: Causes of neutropenia in children

Causes	Number	P value
Bacterial	54	0.01
Viral	20	
Fungal	15	
Drugs	10	
Autoimmune	5	

Table II, graph I shows that main cause of neutropenia was bacterial in 54, viral in 20, fungal in 15, drugs in 10 and autoimmune in 5 cases. The difference was significant ($P < 0.05$).



Graph 1: Causes of neutropenia in children

Table 3: Outcome of cases

Outcome	Number	P value
Live	98	0.02
Death	6	

Table III shows that out of 104 patients, 98 survived and 6 died. The difference was significant ($P < 0.05$).

Discussion

The differential diagnosis for a fever of unknown origin is expansive, but it can be classified into 4 major categories related to underlying etiology: 1) infection; 2) autoimmune/connective tissue disease; 3) malignancy; and 4) allergic/reactive. Other and less common etiologies

including granulomatous and congenital diseases can also be considered [6]. Infections represent the most common causes of fever, although the likelihood of a specific agent varies across geographic location, exposure history, and inherent patient characteristics including age, gender, and race. Autoimmune and connective tissue diseases such as systemic lupus erythematosus and vasculitis are also commonly encountered causes of fever. Among the malignancies, lymphoma, in particular non-Hodgkin lymphoma [7]. The present study evaluated cases of neutropenia and fever in children.

In present study, age group 10-12 years had 14 boys and 8 girls, 12-14 years had 20 boys and 10 girls and 14-16 years had 30 boys and 12 girls. Dubey *et al.* [8] in their study out of 56 patients, males were 30 and females were 26. Etiology of fever was bacteremia in 25, viral URI in 13, GI infection in 4, pneumonia in 7, fungal infection in 4 and others in 3. The difference was significant ($P < 0.05$). The mean duration of fever in males was 1.5 days and in females was 1.8 days, duration of hospitalization in males was 4.2 days and in females was 3.7 days, mortality within 2 weeks in males was 5 and in females was 2. The difference was significant ($P < 0.05$).

We observed that main cause of neutropenia was bacterial in 54, viral in 20, fungal in 15, drugs in 10 and autoimmune in 5 cases. Out of 104 patients, 98 survived and 6 died. Ren *et al.* [9] reported a case in a 22-year-old African-American male with chief complaint of episodic fever. Patient has experienced episodic fevers regularly for the past 6 months. Initially, the fevers occurred 4-6 weeks apart but have been increasing in frequency in the past 2 months. Each episode reportedly lasts about 3 days, with the fever peaking around 103°F. The fever is accompanied by muscle pain and occasionally sore throat, chills, and night sweats. There is no associated nausea, vomiting, or lymphadenopathy. During the previous 3 weeks, the patient reported a decreased appetite and an unintended weight loss of 10-20 pounds. The fevers typically resolved with acetaminophen, and the patient recently completed several courses of amoxicillin.

Chronic autoimmune neutropenia of infancy and early childhood is a relatively common disorder and virtually always runs a benign course, despite very low ANC's. It usually resolves spontaneously by age 3-5 years, with a mean duration of 17 months. In most cases, neutropenia is detected during the occurrence of an acute febrile illness [10]. With follow-up, the neutropenia persists after resolution of the illness that led to testing. Systematic studies indicate that many, but not all, of these children have autoantibodies directed against surface antigens of neutrophils. From a clinical perspective the value of testing for autoantibodies in patients with moderate to severe neutropenia without evidence of recurrent fevers or infections is debatable [11]. Testing is not widely available and, if done, it is best performed by a reference laboratory performing these assays frequently. Serial testing may give inconsistent results and patients with genetic as well as acquired neutropenia may have false positive test results [12].

Griffin *et al.* [13] found that out of 337 FN episodes, infection was proven in 86 (25%) and probable in 75 (22%). 177 episodes (53%) were judged fever of unknown origin (FUO). Bacteremia accounted for most (41) of the proven bacterial episodes, with viridans streptococci (13), Pseudomonas spp (6) and E. coli (6) the most frequently

isolated organisms. The median time to positivity of blood cultures was 12 hrs (range 5.4 - 143.7) with 93% positive within 24 hours of incubation. Viral pathogens were identified in 29 (34%) episodes. Compared to other patients, those with FUO had shorter median duration of fever.

In older children, chronic autoimmune neutropenia or multiple immune cytopenias should raise suspicion of a congenital immunological disorder such as autoimmune lymphoproliferative syndrome or common variable immunodeficiency^[14]. Screening for these disorders can be performed by measurement of circulating T cell receptor alpha/beta positive, CD4/CD8 double negative T cells or of serum immunoglobulins, respectively. Definitive diagnosis of these conditions requires specialized immunological testing^[15].

Conclusion

Authors found that maximum cases were seen in boys and age group 14-16 years.

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